REMARKS

Claims 1, 2, 30, and 31 have been amended to replace the term "standard conditions" with the phrase "stringent hybridization and stringent washing conditions." Support for this amendment is found in the specification at, for example, page 16, lines 1-15.

It is submitted that no new matter has been introduced by the foregoing amendments.

35 U.S.C. § 112, Second Paragraph, Rejections:

Claims 1-3, 20-22, 25-26, and 29-31 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. (Paper No. 20060705 at 2).

In making the rejection, the Examiner asserted that the phrase "hybridizes under standard conditions" renders the claims indefinite. (*Id.*). The Examiner further asserted that "[t]he claims do not explicitly state the conditions which Applicants call 'standard.'" (*Id.* at 2-3). The Examiner also asserted that "Applicants refer to Sambrook in an exemplary way and do not quote any page presenting the conditions. It is unknown what conditions considered "standard" in the art are included and/or excluded from the scope of the claims." (*Id.* at 3).

Initially, we note that claim 26 has been previously cancelled; therefore, the rejection is moot as to claim 26.

With a view towards furthering prosecution, claim 1 (from which claims 2-3, 20-22, 25, 28, and 29 depend), claim 30, and claim 31 have been amended to replace the term "standard conditions" with the phrase "stringent hybridization and stringent washing conditions." The specification as filed provides details as to how this

phrase is to be interpreted, *see*, *e.g.*, page 16, lines 9-15. For exact details of these hybridization procedures, the specification cites to Sambrook *et al.*, Molecular Cloning (2nd ed.), Cold Spring Harbor Laboratory Press 1989, New York. For example, Sambrook provides on page 9.52 a complete protocol for stringent hybridization and stringent washing conditions. A copy of this protocol is attached as Exhibit 1.

In view of the amendments and the disclosure in the specification to look to Sambrook for the particulars of the high stringency wash and hybridization, it is respectfully submitted that one skilled in this art would readily understand the scope of the claims.

For the reasons set forth above, it is believed that the rejection of claims 1-3, 20-22, 25, and 29-31 is rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

35 U.S.C. § 112, First Paragraph, Rejections:

Claims 1-3, 20-22, 25, 28, and 30-31 have been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. (Paper No. 20060705 at 3).

In making the rejection, the Examiner asserted that "the disclosure does not teach the hybridization conditions to be used in selection of DNA molecules of [the] invention, [and therefore] claims 1-3, 20-22, 25, 28, 30-31 as amended are not enabled and thus rejected." (*Id.* (original emphasis)).

In response to Applicants' remarks submitted April 20, 2006, the Examiner stated: "Applicants['] emphasize that the degree of homology between the enzymes disclosed and identified as SEQ ID NO: 5, 6, 7, and 8 is at least 80%, and any known alcohol dehydrogenase activity was in the range of 26 to 31%." (*Id.* at 3). The

Examiner then stated that: "Applicants' argument has been fully considered but is found not persuasive, because it is an argument pertaining to the question of existence of prior art, and not the question of enablement." (*Id.* at 4).

Initially, we note that it is the Examiner's burden to demonstrate that a specification is not sufficiently enabling. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). To carry her burden, the Examiner must identify and clearly articulate the factual bases and supporting evidence that allegedly establish that undue experimentation would be required to carry out the claimed invention. *Id.* at 370.

With a view towards furthering prosecution, claim 1 (from which claims 2-3, 20-22, 25, 28, and 29 depend), claim 30, and claim 31 have been amended to replace the term "standard conditions" with the phrase "stringent hybridization and stringent washing conditions."

We note that the phrase "hybridizes under stringent hybridization and stringent washing conditions" is an art-recognized phrase that one skilled in the art would understand, even without further guidance from the specification. However, as discussed above, the specification as filed (at page 16, lines 9-15) discloses how this term is to be interpreted by reference to the art recognized Sambrook book. It is respectfully submitted that one skilled in the art armed with the presently amended claims, the specification, and Sambrook would have very quickly found on page 9.52 of Sambrook a complete protocol for stringent hybridization and stringent washing conditions as disclosed and claimed. For the preparation of the hybridization solution, Sambrook also discusses on page 9.47, item 1, that aqueous solutions and solutions of 50% formamide are both solvents that show excellent results. Therefore, the Examiner's statement that "the disclosure does not teach the hybridization conditions to

be used in selection of DNA molecules of [the] invention" is ***misplaced.*** (Paper No. 20060705 at 3). For this reason alone, the rejection should be withdrawn.

Moreover, the specification discloses that the nearest homologues of Enzyme B (SEQ ID NO: 8) exhibit a maximum homology of 26-31% with known enzymes (page 34, line 20 to page 35, line 4):

> Homology search of Enzymes A, A', A" and B revealed that Enzymes A, A', A" and B showed rather low homology (26-31% homology through the polypeptides) with several quino-proteins including alcohol dehydrogenase of *Acetobacter aceti* (T. Inoue et al., J. Bacteriol. 171: 3115-3122) or *Acetobacter polyoxogenes* (T. Tamaki et al., B.B.A., 1088: 292-300), and methanol dehydrogenase of *Paracoccus denitrificans* (N. Harms et al., J. Bacteriol., 169: 3966-3975), *Methylobacterium organophilum* (S.M. Machlin et al., J. Bacteriol., 170: 4739-4747), or *Methylobacterium extorquens* (D.J. Anderson et al., Gene 90: 171-176).

One skilled in the art would immediately recognize that the DNA encoding such known enzymes would ***not*** hybridize under "***stringent hybridization and stringent washing conditions***" to the DNA encoding SEQ ID NO: 8 (*i.e.*, a DNA according to SEQ ID NO: 4). Thus, such known enzymes would not fall within the scope of the currently claimed subject matter.

Table 7 of the specification details the degree of homology between the AADH (Alcohol/Aldehyde Dehydrogenases) of SEQ ID NO: 8 and three other amino acid sequences having AADH activity, *i.e.*, SEQ ID NOS: 5, 6 and 7, which are disclosed throughout the specification. The results in Table 7 demonstrate that a homology of at least 80% was detected:

Table 7. Homologies of amino acid sequences among AADHs.

	Enzyme A	Enzyme A'	Enzyme A"	Enzyme B
Enzyme A	100	_	_	_
Enzyme A'	89	100	_	_
Enzyme A"	85	86	100	_
Enzyme B	83	82	81	100

(See specification at page 34, lines 15-20). As discussed above, the next highest homology between Enzymes A, A', A", and B to enzymes with known alcohol or methanol dehydrogenase activity was in the range of 26 to 31%. (See Specification at page 34, line 20 to page 35, line 4). Thus, the data in Table 7 clearly provides evidence that the Applicants enabled the full scope of the amended claims by unambiguously identifying enzymes having highly homologous polypeptide sequences and sharing a common function -- AADH activity.

The Examiner's statement that "Applicants' argument has been fully considered but is found not persuasive, because it is an argument pertaining to the question of existence of prior art, and not the question of enablement" is not understood. (Paper No. 20060705 at 4). The previous argument made no reference to any prior art. Rather, the argument pertained to and still pertains to the degree of experimentation needed to identify enzymes having highly homologous polypeptide sequences and sharing AADH activity.

As is well accepted, even a "considerable amount" of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance. MPEP § 2164.05 and *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Here, the specification provides ample guidance, both by disclosing the degree of

homology between the AADH of SEQ ID NO: 8 and three other amino acid sequences having AADH activity, *i.e.*, SEQ ID NOS: 5, 6 and 7 and by requiring "stringent hybridization" and "stringent washing conditions." Accordingly, it is respectfully submitted that undue experimentation would not be required to carry out the currently claimed invention. For this additional reason, this rejection should be withdrawn.

Claims 2-3 have also been rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. (Paper No. 20060705 at 4).

In making the rejection, the Examiner asserted that claims 2 and 3 "do[ ] not reasonably provide enablement for an enzyme that comprises a combination of at least two amino acids sequences each of said sequences being selected from the group of SEQ ID NO: 8 and SEQ ID NO: 5 and amino acid sequences encoded by DNA sequences hybridizing under standard conditions with DNA molecules according to SEQ ID NO:4 or 1." (*Id.* (original emphasis)). The Examiner, however, acknowledged that claims 2 and 3 are "enabling for the plasmid comprising genes encoding SEQ ID NO: 5 and SEQ ID NO: 8 (plasmids pSSAB201 and pSSBA201)." (*Id.*).

In response to Applicants' remarks submitted April 20, 2006, the Examiner stated "without further guidance on the part of Applicants related to the structure of chimeric enzymes, one skilled in the art is forced to construct numerous combination[s] of disclosed sequences and/or sequences that are hybridizing to SEQ ID NO:1 or SEQ ID NO:4 under indefinite conditions, ..." (*Id.* at 5 (original emphasis)). The Examiner further stated that "[t]he figures are schematic and for that reason do not identify the details of structure, i.e., sequences, of claimed hybrid molecules." (*Id.*).

With a view towards furthering prosecution, claims 2 and 3 have been amended. Claim 1 (from which claims 2 and 3 depend) has been amended to recite

"stringent hybridization and stringent washing conditions" instead of "standard conditions." Therefore, the Examiner's concern regarding "indefinite conditions" has been rendered moot. (*Id.*)

In view of this amendment, we note that the construction of the currently claimed chimeric nucleic acid molecules and polypeptides is enabled and specifically disclosed in the specification at, for example, Examples 14 and 15 and in Figures 2, 3, 4, 7, and 8. The Examiner's statement that "figures [2, 3, 4, 7, and 8] are schematic and for that reason do not identify the details of structure, i.e., sequences, of claimed hybrid molecules" misses the point. (*Id.*). These figures must considered, not in isolation, but in conjunction with the specification as a whole and what one skilled in the art would learn from them. For example, the specification discloses the enzymatic activity of these constructs (*see, e.g.*, Figure 11). Furthermore, the specification also discloses in Tables 11 and 12 comparisons of the substrate specificities of the claimed enzymes. In view of the amended claims, the extensive disclosure in the specification, as well as the above-identified Tables and drawings, one skilled in this art would have been able to make and use what is claimed. Thus, the skilled person is ***not*** left "without a[ny] further guidance" as asserted by the Examiner. (Paper No. 20060705 at 5). In sum, the specification clearly enables the full scope of the currently claimed chimeric enzymes (*i.e.*, the chimeric enzymes identified as Enzyme B (*i.e.*, SEQ ID NO: 8) and Enzyme A (*i.e.*, SEQ ID NO: 5) and the chimeric enzymes encoded by DNA sequences hybridizing under "stringent hybridization and stringent washing conditions" with DNA molecules according to SEQ ID: 4 or 1).

In view of the foregoing, it is respectfully submitted that the rejection has been rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

For the foregoing reasons, favorable action on the merits, including entry of the amendments, withdrawal of the rejections, and allowance of all the claims, respectfully are requested. If the Examiner has any questions regarding this paper, please contact the undersigned attorney.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box. 1450 Alexandria, VA 22313-1450, on January 12, 2007.

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